American Journal of Medical Genetics 70:121–129 (1997)

Acceptance of Home and Clinic-Based Cystic Fibrosis Carrier Education and Testing by First, Second, and Third Degree Relatives of Cystic Fibrosis Patients

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We contacted and offered free cystic fibrosis (CF) carrier education and testing to the first, second, and third degree relatives of individuals with CF followed at a large Southeastern US CF Clinic. Relatives were offered CF carrier education and testing either in their homes or in a genetic counseling clinic. Overall, of 514 relatives offered free CF carrier education and testing, 299 (58%) accepted. Significantly more (67%) of those offered education and testing in their homes accepted than those offered education and testing in a genetic counseling clinic (45%).

Regression analyses identified several factors, including education, income, gender, perceived chance of being a carrier, and perceived chance of having a child who is a CF carrier, as predictors of acceptance of education and testing in both home and clinic sites. A smaller set of factors was identified that predicted acceptance of education and testing unique to each site.

Within the limits of this study and its design, even when CF carrier testing is offered free of charge, including education and testing in the home, acceptance of education and testing, while higher than in general population samples, is not universal among at-risk relatives. Several factors which may have contributed to the observations reported in this study are discussed. Am. J. Med. Genet. 70:121–129, 1997.

KEY WORDS: CF carrier testing; genetic education; carrier testing relatives; genetic counseling

INTRODUCTION

Since identification of the gene, gene product, and major mutation responsible for cystic fibrosis (CF) in 1989 [Riordan et al., 1989], more than 450 additional mutations have been identified. At the present time, a panel of 6 of the most common mutations can detect between 75 and 85% of CF carriers in the general U.S. population [U.S. Congress, 1992]. Earlier carrier screening efforts in this country, such as for Tay Sachs, sickle cell, and thalassemia traits, were limited largely to specific ethnic or minority groups [Holtzman, 1989]. In contrast, CF is most prevalent in the largest population segment, Caucasians, and while not all carriers can be identified, discovery of the major mutation brought the potential for screening millions.

Shortly after identification of the major mutation responsible for CF, a number of professional groups expressed concern about mass CF carrier screening because of its limitation in identifying all carriers, as well as concern about a possible overwhelming demand for screening [American College of Obstetrics and Gynecology, 1992; American Society of Human Genetics, 1992]. They called for a moratorium on population-based screening programs until pilot studies could be conducted to assess demand and explore ways of providing effective education and screening. In these discussions it was noted that carrier testing should be

Contract grant sponsor: National Center for Human Genome Research, National Institute of Health; Contract grant number: RO1-HG00643.

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Received 8 February 1996; Accepted 18 September 1996

offered to individuals and couples with a family history of CF [National Institutes of Health 1990]. In such families the test can be virtually 100% informative for blood relatives if the particular family mutations are known. However, it was not clear if such testing was being offered to relatives and what percent of at-risk relatives would in fact accept direct mutation CF carrier testing.

A significant concern expressed about CF carrier screening was that the demand for it among both the population at large and in particular among at-risk relatives could overwhelm the capacity of the health care system to offer adequate education, testing, and counseling. Few empirical studies have examined the demand for or the decision to have carrier testing among relatives of individuals with CF. Four studies do report the attitudes of relatives toward CF carrier testing. Denayer et al. [1992] studied 109 aunts and uncles of individuals with CF and found that three fourths said that if offered a carrier test they would accept it. Miller and Schwartz [1992] found wide variation among members of 3 religious groups in their approval of CF carrier testing. For example, whereas 60 and 48% of Mennonite and Amish approved of CF carrier testing, respectively, only 31% of Hutterites did. Watson et al. [1991] asked 238 relatives of individuals with CF if they would make use of a carrier test should it become available and 89% reported that they would. Finally, Wolff et al. [1990] asked 23 relatives of individuals with CF if they would want to know the results of a carrier test and 91% reported they would.

Several studies report on relative's decisions to be tested, based on either linkage or direct mutation testing. Miller and Schwartz [1992], in the study cited above, asked relatives who had participated in a linkage-based carrier testing program if they wanted to know their test results. Just under 80% reported they did. Turner et al. [1993] employed an active outreach method of recruiting relatives for CF carrier testing. They contacted and provided written materials about carrier testing and direct mutation testing to 230 descendants of a couple who were presumed to carry the ΔF508 mutation. They report that just over 75% agreed to be tested. In another study, Surh et al. [1994] used a method of offering testing that relied on family members to inform relatives that they were at risk of being a carrier and of the availability of carrier testing. They report that this approach resulted in less than 10% of the parents, sibs, grandparents, aunts, uncles, first cousins, and other more distant relatives seeking carrier testing. Finally, Fanos and Johnson [1995], in a study of 54 adult sibs and their 30 spouses, identified several barriers to CF testing, including 1) difficulty in learning about the availability of testing, 2) lack of communication within the family and among CF sibs about carrier testing, as well as 3) family myths about carrier status that discouraged testing. They argue that remaining ignorant about one's CF carrier status can perform several psychological functions for adult sibs of CF patients.

The observation that relatively large percents of at-risk individuals report hypothetically they would be tested is consistent with research on other types of genetic carrier and even susceptibility and presymptomatic testing [Croyle and Lerman, 1995]. Studies of actual testing uptake report wide variability, however. Also, comparison of the Turner and Surh experiences suggests that approaches which rely on professionals directly contacting relatives may result in higher acceptance rates than studies which rely on people with CF or their parents contacting relatives.

We undertook a pilot CF carrier testing program that offered education about carrier testing to first, second, and third degree relatives of individuals with CF and provided free testing and, if positive, free genetic counseling for relatives accepting the offer. The major objectives of our pilot testing program were to 1) compare the level of acceptance of CF carrier education and testing when offered to be done in the home with the level of acceptance of CF carrier education and testing when offered to be done in a genetics clinic, and 2) compare the educational effectiveness and psychosocial impact of CF carrier education and testing in these two settings. In this paper we report data on the first objective.

METHODS

Approach and Rationale

Genetic carrier testing can be viewed as consisting of a) pretest education in which people are given information enabling them to understand the testing process and to make an informed decision about testing; b) collection of a biological sample from the person, often blood, but sometimes saliva; c) reporting the results of the test to the individual; and d) genetic counseling. Sometimes steps a and b occur together as can steps c and d. There is consensus that counseling by a genetic counselor should be offered to all tested individuals who request it and especially for those who test positive as a carrier [National Institutes of Health, 1990].

The present study reports the results of a randomized trial comparing the acceptance of home-based and genetic clinic-based CF carrier education and testing by relatives of individuals with CF. We were interested in examining the acceptance of carrier education and testing in these 2 settings because they constitute divergent models of how the education and testing components of an overall carrier testing program might be provided. On the one hand, home-based education and testing offer the maximum in convenience by removing not only travel and scheduling barriers, but also by removing the costs associated with travel and perhaps time off from work. On the other hand, the clinic offers the reassurance that may come from face-to-face contact with a health professional and the opportunity to discuss issues of particular interest or concern to the individual. There are major differences in both the health personpower as well as health costs associated with each approach. For example, should demand be great, home-based education and testing, if comparably effective with clinic-based education and testing, could significantly reduce both the burden on genetic professionals to provide these services as well as the overall costs of the entire carrier testing experience.

Here, in addition to noting the percent of relatives who accept education and testing at each site, we report the number of carriers identified and the number of spouses/partners tested. Finally, exploratory logistic regression methods are used to develop models of factors predicting the acceptance by relatives of education and testing at each site.

Study Population

The population for this study all had a relative with CF who was being followed at a large CF Center in the southeastern United States. The Center, established in 1975, is located in a medical complex in a suburban setting and is a designated Cystic Fibrosis Foundation Center. Four hundred and twenty-seven proband families were identified through the CF Center patient roster. A letter from the CF Clinic Director was sent to CF patients, or to their parents if the patients were minors, describing the study and asking if they would be willing to provide 1) a family pedigree, 2) the addresses and phone numbers of relevant first, second, and third degree relatives, and if necessary, 3) a saliva sample to determine the specific CF mutations in the family. The letter explained relatives would be offered free CF carrier education, testing, and counseling and relatives could decline acceptance if they so desired. The letter explained that a research project person would contact them in a few days.

During the follow-up telephone call to the proband family contact by the project interviewer, questions about the study by the probands or their parents were answered and they were asked if they would assist in identifying relatives. The interviewer had special training about CF and genetic issues surrounding CF carrier testing in families. A genetic counselor was available who could call CF patients and/or their parents if they had questions or if they simply asked to speak to a genetic counselor. No one requested to speak to the genetic counselor. Family contacts were informed that if they agreed to provide contact information, we would inform their relatives that we had obtained the names and contact information from them [Sorenson et al., 1996].

Of the 427 proband families identified in the CF Clinic population, 80 (18.7%) lived outside the study inclusion area (North Carolina, South Carolina, Tennessee, Virginia, West Virginia). An additional 27 (6.3%) were excluded because they were in another research project, there was an unclear CF diagnosis, the proband did not have one of the 6 mutations being tested for in this study (ΔF508, G542X, G551D, R553X, W1282X or N1303K), or no contact information on the family was available. Of the remaining 320 families, 68 (21.3%) could not be reached by telephone. An additional 49 (15.3%) reported no eligible relatives living in the study catchment area. Of the remaining 203 families, 109 (53.7%) provided a pedigree and contact information on their relatives and, if necessary, a saliva sample for identifying the specific CF mutations in the family. An additional 33 (16.4%) family contacts agreed to participate, but did not provide contact information on relatives and/or a saliva sample for mutation testing if requested. Sixty-one (30.1%) refused to participate altogether when first contacted.

A total of 1,648 first, second, and third degree relatives were identified by the 109 CF family contacts. On average, each contact person identified just over 15 relatives with a range from none to 99. Just under 60%, 949, of the identified relatives did not meet study inclusion criteria (residency in one of the five states listed above, 18 years of age or older, CF carrier status unknown, not pregnant, and able to be reached by telephone) or the family could not provide contact information on relatives. This left 699 of the initial 1,648 relatives identified by probands or their parents eligible for contact by the study.

Subject Recruitment

All relatives received a letter from the project informing them about the purpose of the study and indicating that if they chose to participate they would receive at no cost CF carrier education, testing, and genetic counseling. They were also informed that if they tested positive and had a spouse or partner, free CF carrier education, screening, and genetic counseling would be offered to the spouse. Along with the letter, relatives were provided with a detailed informed consent statement. The statement discussed the purpose of the study; activities required for participation in the study; potential benefits and risks of involvement in the study; confidentiality issues, including possible requests in the future from insurance companies and employers concerning their CF carrier status; and the accuracy of testing. The study was reviewed and approved by the local institutional review board.

Approximately 10 days after sending the letter, the project interviewer contacted all relatives by telephone to ask if they had received and read the letter and informed consent statement. The interviewer answered any questions the relatives had about the study. They were then asked if they wanted to accept CF carrier testing. Relatives were recruited as individuals, not as members of an extended CF family. Accordingly, although subjects may have known we were contacting other relatives in their family, we did not share with them any information about the participation of their relatives.

Of the 699 eligible relatives, we were unable to contact 151 (21.6%) by telephone or they did not make a decision about participation in the study if contacted. An additional 34 (4.9%) were found to be ineligible when contacted. This left 514 relatives who made a decision whether to participate. Figure 1 summarizes both the number of CF family contacts as well as the relatives in the study.

Education and Testing Arrangements

Home-based education and testing consisted of two parts. First, relatives in the home-based carrier education and testing site (N = 309) were mailed a CF carrier pamphlet developed especially for this project [Testing for Cystic Fibrosis Carriers, 1992]. The pamphlet, written at a sixth grade level, provided information on the disease, how the disease is inherited, CF

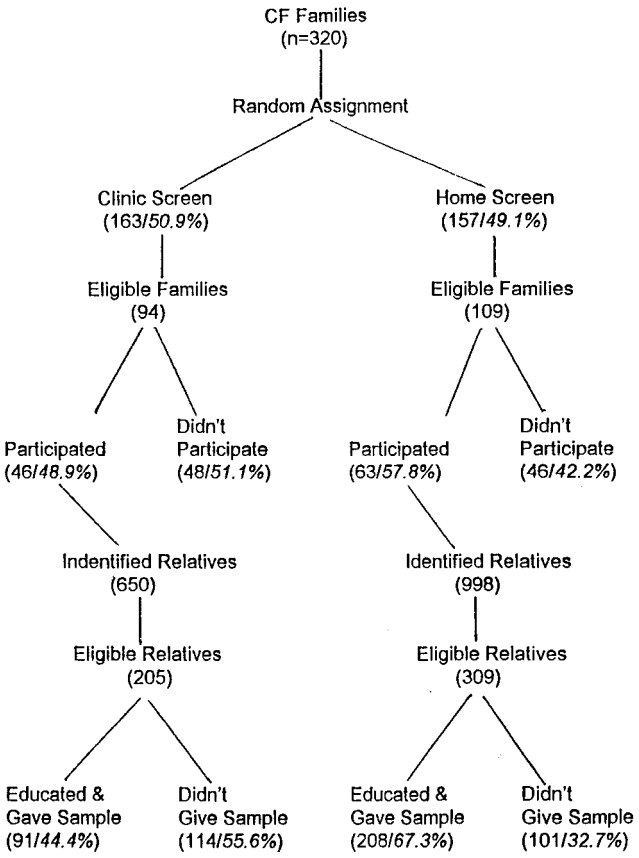

Fig. 1. Study flow chart.

carrier status, the carrier risk to relatives, the absence of known health consequences of CF carrier status, and the reproductive implications of carrier status.

Along with the CF carrier pamphlet, home-site testing relatives received a kit for providing a buccal cell sample. The kit consisted of a letter instructing the relatives how to provide the sample using a saline rinse and a tube with a pouch for return mailing. Relatives were informed that it would normally take about 4 weeks to process the sample and that they would be informed about the results by a telephone call from the interviewer, followed by a letter.

Relatives assigned to the genetic clinic education and testing arrangement (N = 205) also received a letter from the project along with the informed consent statement. In a follow-up telephone call, relatives who accepted the offer of CF carrier testing were scheduled for a clinic visit. Once at the clinic, relatives were provided with CF carrier education by a genetic counselor. The counselor used the CF pamphlet as the protocol for guiding the educational session. The face-to-face interaction in addition allowed for relatives to ask questions and pursue issues of personal concern to them. After the educational session, which lasted on average about 30 minutes, relatives were asked to provide a saliva sample and were told that it normally took about 4 weeks for the results to be reported.

Data Collection

Data were collected from 5 primary sources: a) the CF Center patient roster; b) CF Foundation Patient Registry forms; c) structured recruitment telephone interviews with both family contacts as well as relatives; d) pedigree charts gathered from family contacts; and e) questionnaires completed by relatives prior to being tested, while waiting for the results of their test, immediately after receiving their results, and again one, 6, and 12 months after testing and genetic counseling. The questionnaires collected standard sociodemographic information and contained closed-ended questions to assess knowledge, attitudes, beliefs, and selected health behaviors concerning CF and CF carrier status. They also contained several psychological scales that allowed assessment of the relatives' affective state. The data reported here come from all 5 sources, but not from the questionnaires administered while relatives were waiting for results, or immediately and one, 6, and 12 months after testing and counseling. These data are reported elsewhere [Cheuvront et al., 1997].

RESULTS

Randomization

Prior to contacting relatives, the 320 CF families were randomly sorted for order of entry into the study. The families were then randomly assigned to one of the 2 education and testing sites: 163 families to the clinic site and 157 families to the home site. This assured that all the relatives within an extended CF family would be offered the same education and counseling site. Because CF families, not individual relatives, were randomly assigned to sites, assessment of the efficacy of the randomization procedure was based on CF family, CF patient, and extended CF family characteristics, not individual relative characteristics.

Of the 109 CF families in which relatives accepted the offer of education and testing, 46 had been assigned to the clinic site and 63 to the home site. These 2 sets of families were compared on the following variables: sex of the CF patient, source of patient clinic care (adult vs. pediatric), length of time patient had a CF diagnosis, number of patient clinic visits and hospitalizations in 1993, need for CF family mutation testing, total number of relatives eligible for testing, and total number of relatives willing to complete a questionnaire, regardless of their decision to be tested. Chi square analysis revealed no statistically significant differences between the clinic and home families on these characteristics, suggesting effective family randomization.

Subjects

Table I reports characteristics of the 514 relatives offered CF carrier testing. Few were over 45, had household incomes greater than $50,000 per year, or college experience beyond the baccalaureate degree. Just under two thirds were currently married. All of the relatives were Caucasians. Ninety percent were

Protestants, mostly Baptists or Methodists, and only 1.3% Catholic or Jewish. Only 5.6% were sibs of the person with CF. This is largely due to the majority of CF patient sibs being under 18 and therefore excluded from the study. Contact with the CF patient varied, but few reported no contact. Just under one third of the relatives were planning a child in the future, and just over one third believed that raising a child with CF would constitute a high burden. Nearly 90% reported they would not abort a fetus diagnosed with CF. Although all relatives had at least a one in 4 chance of being a carrier, comparatively few saw themselves as having a high risk. Almost two thirds of the relatives either provided no estimate of their chance or thought that it was less than 1%. Only 3.1% accurately reported their precise risk.

TABLE I. Sociodemographic Characteristics of Participants

N		Percent
514	Gender	
	Male	48.2
	Female	51.8
454	Age (years)	
	18–25	27.1
	26–45	55.7
	46+	17.2
425	Annual household income	
	≤$20,000	48.0
	$20,001–$50,000	45.4
	≥$50,001	6.6
432	Education	
	≤High school diploma	52.5
	<Four-year college degree	28.7
	≥Four-year college degree	18.8
487	Marital status	
	Married	65.7
	Never married	23.6
	Currently divorced	6.4
	Widowed, separated, cohabitating	4.3
514	Relationship to CF relative	
	Sib	6.6
	Aunt	30.0
	Uncle	24.7
	Female cousin	17.7
	Male cousin	19.8
	Niece/nephew	1.2
514	Related to CF relative through	
	Mother's side of the family	43.4
	Father's side of the family	48.8
	Both sides of the family	7.8
456	Frequency of contact with the CF relative	
	≥Weekly	30.9
	≥Monthly	27.9
	≤Yearly	31.8
	No contact	9.4
453	Planning to have a child in the future	
	Yes	31.3
	Not sure	8.8
	No	59.8
437	How burdensome it would be to raise a child with CF disease	
	Low	20.1
	Moderate	44.4
	High	35.5
430	Willing to abort a fetus known to have CF	
	Yes	10.5
	No	89.5
456	Perceived chance of being a CF gene carrier	
	High, very high	14.7
	Moderate	34.9
	Low, very low	46.3
	No response	4.2
456	Estimated risk of being a CF gene carrier	
	No response	17.1
	1 in 1 to 1 in 9	18.9
	1 in 10 to 1 in 99	21.9
	1 in 100 to 1 in 999	19.7
	1 in 1,000 or less	22.4

Data Analyses

Individual relatives do not constitute totally independent units for statistical purposes. Membership in a particular family, with its unique experience with CF, may lead to a shared view of the disease. Also, it is likely that over the years, relatives discussed CF among themselves, including carrier testing and, hence, this may have had an effect on their decisions concerning testing. Accordingly, analyses were performed using data from relatives clustered by membership in their respective families. Variables which described the family (size, number of CF patients) were assigned to each relative within the family. All analyses were performed using SUDAAN software, version 6.34 [RTI, 1993]. These computing procedures allow intraclass correlations among relatives in the same family to be taken into account in standard errors for estimates, statistical tests, and confidence intervals.

Participation by Testing Site

Of the 514 relatives offered CF carrier testing, 299 (58%) chose to be tested. Slightly less than 45% of the 205 relatives offered clinic education and testing accepted, compared to just over 67% of the 309 relatives offered home-based education and testing. The difference in the percent of relatives in the 2 groups who accepted testing is statistically significant ($\chi^2_{(1,514)} = 6.939$, Fisher's exact test (2-tail), $P < .01$, OR 2.58, CI [1.36–4.90]). In sum, relatives from families offered home-based pamphlet education and testing were significantly more likely to accept testing than were those relatives offered clinic-based education and testing.

Carrier Detection

Phosphate-buffered saline mouthwash was used as a source of buccal epithelium cells for both the home and clinic populations [Gilfillan et al., 1994]. After centrifugation, DNA was extracted by standard methods and mutation analysis was performed using a reverse dot-blot format [Courtesy Roche Molecular Systems, Alameda, CA] following polymerase chain reaction (PCR) amplification for the 6 mutations assessed in this project. All positive results were confirmed by an independent method [Friedman et al., 1991]. Amplification failure was seen in less than 10% of samples. Repeat amplification of these samples was successful in approximately 50% of amplification failures. Less than 5% of subjects had to be resampled.

A total of 120 (40.1%) of the 299 relatives tested positive for the specific mutation in their family. Ninety

percent had the ΔF508 mutation. Of the 91 relatives in the clinic setting who were tested, 36 (39.6%) had a positive carrier test and of the 208 relatives in the home-based education and testing setting, 84 (40.4%) tested positive for the CF mutation in their family. Of the remaining 179, 3 had inconclusive test results and 3 could not be contacted by telephone. In each of these latter 3 cases, an attempt was made to locate the participant through other relatives. If necessary, a registered letter was sent to their last known address asking them to contact us for their test result.

Among the 120 relatives who tested positive, 92 reported having a spouse/partner. Of these 92 partners, 63 (68%) accepted the offer of education and testing. We identified 58 carrier by "noncarrier" couples. These couples were offered free genetic counseling at the genetic clinic. Seventeen (29%) accepted the offer for free genetic counseling. The most frequently cited reasons for not accepting counseling among the carrier by noncarrier couples were 1) they were planning no more children and felt they did not need counseling and 2) problems in scheduling genetic counseling because of clinic hours or because of their personal schedules, usually work. The counseling of the 17 couples covered the standard topics of genetic counseling and included attention to the fact that a noncarrier result could not be equated to not being a carrier with total certainty. We also identified a total of 5 carrier by carrier couples. These couples were removed from the study protocol and immediately offered standard genetic counseling for CF carrier couples.

Regression Analyses

Of the 514 relatives who made the decision of whether to be tested, 58 who did not want to be tested also refused to provide any information in the interviews and questionnaires. Since all information was missing on these relatives other than their testing decision, they were excluded from regression modeling. In addition, some of the remaining 456 relatives chose not to or were unable to answer some questions. To avoid losing such data from these relatives, bivariate analyses were performed treating the missing data on these relatives as a separate category of responders. The missing data category on variables for these relatives was assigned the value of the category of responders who acted statistically similar to them in relation to the major outcome variable, accepting or not accepting education and testing. This strategy maximized the data and relatives for the regression analyses.

Regression modeling began by assessing bivariate relationships between being tested and family and relative type variables. The selection of variables to be included in this analysis was based on a) known empirical predictors of participation in medical screening programs generally, such as education and income [Cockerham, 1978], as well as on variables for which there was a priori theoretical rationale to expect they would be predictors of the decision to be tested, such as perceived burden of CF disease and perceived chance of being a CF gene carrier [Genetic Screening, 1975].

Table II lists the relationships which were statistically significant in the bivariate analysis. A general stepwise logistic regression analysis was performed allowing all variables which had significant bivariate relationships with the outcome variable to act as candidate variables for the model. This initial logistic regression model identified 9 variables that were predictors of the decision to accept education and testing. The variables which predicted being tested were 1) planning additional children; 2) higher household income level; 3) higher level of education; 4) being female; 5) perceived increased chance of being a carrier; 6) perceived increased chance of having a child who would be a CF gene carrier; 7) proband care provided in the pediatric CF Clinic; 8) reduced driving time to the genetic clinic for education and testing, and 9) having a spouse or partner. This 9-variable model achieved a Goodman-Kruskal gamma of 0.587, suggesting good model stability and predictability.

To determine whether or not one model fit equally those relatives assigned to the clinic and home-testing sites, the variables from the initial model were forced into a second model. Interactions of each of the model variables with testing location assignment were added, but only the interactions were allowed to exit the model through backward elimination. Any statistically significant interactions would suggest that the initial model variables behaved differently when comparing clinic vs. home-testing sites and separate models would be needed for each. Three of the variables had significant interactions with the testing site: 1) having a spouse or partner; 2) medical care received by the CF patient in the pediatric CF clinic; and 3) length of time to drive to the CF clinic. Accordingly, separate models were developed for each education and testing site.

In the final regression analyses, the variables from the initial model which did not have a significant interaction with the education and testing sites were forced into separate logistic regression analyses for the home and clinic populations. The 3 variables with interactions with education and testing site were allowed to leave the models through backward elimination. CF patient care in the pediatric CF clinic and drive time remained in the clinic model, and having a spouse or partner remained in the home model. Table III provides a summary of the separate models for each education and testing site. The clinic model achieved a Goodman-Kruskal gamma of 0.593 and the home model a gamma of 0.507, suggesting stable and predictable models.

DISCUSSION

The major objective of this study was to assess the acceptance by relatives of individuals with CF of free carrier education and testing in home and clinic sites. In our population of relatives, all of whom had at least a 1 in 4 chance of being a CF gene carrier, 44% of those offered clinic-based education and testing accepted, while 67% of those offered home-based education and testing accepted. These figures indicate, at least under the conditions in which CF carrier education and testing were offered in this study (i.e., contact by research personnel offering the services, no billing to the sub-

TABLE II. Significant Bivariate Relationships With CF Carrier Testing*

	Clinic test	Home test
	% Who gave a sample	% Who gave a sample
CF care clinic		
Adult	$27.5_{(n=69)}$	$58.8_{(n=114)}$
Pediatric	$52.9_{(n=136)}$	$72.3_{(n=195)}$
Degree of relatedness to the CF patient		
First degree	$83.3_{(n=6)}$	$85.7_{(n=28)}$
Second degree	$43.5_{(n=131)}$	$68.0_{(n=150)}$
Third degree	$42.6_{(n=68)}$	$63.6_{(n=131)}$
Related to CF patient through		
Patient's mother	$50.7_{(n=79)}$	$70.1_{(n=144)}$
Patient's father	$37.3_{(n=118)}$	$60.9_{(n=133)}$
Both parents	$87.5_{(n=8)}$	$81.3_{(n=32)}$
Amount of contact with the proband		
Daily	$21.4_{(n=14)}$	$88.0_{(n=25)}$
Once a week	$46.5_{(n=43)}$	$72.9_{(n=59)}$
<Once a month	$45.0_{(n=20)}$	$82.1_{(n=39)}$
Once a month	$62.1_{(n=29)}$	$71.8_{(n=39)}$
<Once a year	$54.2_{(n=48)}$	$58.0_{(n=69)}$
Once a year	$28.6_{(n=7)}$	$42.9_{(n=21)}$
No contact	$33.3_{(n=12)}$	$35.5_{(n=31)}$
Gender of subject		
Male	$39.6_{(n=101)}$	$57.1_{(n=147)}$
Female	$49.0_{(n=104)}$	$76.5_{(n=162)}$
Age of subject		
18–25 years old	$58.8_{(n=51)}$	$77.8_{(n=72)}$
26–45 years old	$53.2_{(n=94)}$	$75.5_{(n=159)}$
>45 years old	$40.1_{(n=27)}$	$60.8_{(n=51)}$
Presence of a spouse or partner		
Yes	$44.4_{(n=151)}$	$71.9_{(n=224)}$
No	$44.4_{(n=54)}$	$55.3_{(n=85)}$
How much of a burden to raise a child with CF		
Low burden	$50.0_{(n=32)}$	$75.0_{(n=56)}$
Moderate burden	$58.1_{(n=74)}$	$79.2_{(n=120)}$
Extreme burden	$48.3_{(n=60)}$	$69.5_{(n=95)}$
Already have children		
Yes	$47.0_{(n=115)}$	$71.9_{(n=185)}$
No	$62.7_{(n=59)}$	$76.0_{(n=96)}$
Planning to have (more) children		
Yes	$64.8_{(n=58)}$	$83.3_{(n=84)}$
Not sure	$72.2_{(n=18)}$	$59.1_{(n=22)}$
No	$42.7_{(n=96)}$	$70.4_{(n=176)}$
Education		
High school or less	$36.4_{(n=66)}$	$65.2_{(n=161)}$
Some college	$58.8_{(n=51)}$	$79.5_{(n=73)}$
Four-year degree[a]	$68.3_{(n=41)}$	$90.7_{(n=43)}$
Household income		
$20,000 or less[a]	$50.8_{(n=61)}$	$62.9_{(n=89)}$
$20,001–$50,000	$51.6_{(n=64)}$	$75.7_{(n=144)}$
>$50,000	$61.0_{(n=41)}$	$87.0_{(n=46)}$
Chance of being a carrier (verbal)		
Extremely high	$20.0_{(n=5)}$	$90.0_{(n=10)}$
High	$72.2_{(n=18)}$	$85.3_{(n=34)}$
Medium	$59.4_{(n=64)}$	$79.0_{(n=95)}$
Low	$53.5_{(n=58)}$	$69.5_{(n=89)}$
Extremely low	$27.8_{(n=18)}$	$65.2_{(n=46)}$
Chance of being a carrier (numeric)		
1 in 1 to 1 in 9	$71.4_{(n=42)}$	$88.6_{(n=44)}$
1 in 10 to 1 in 1,000,000[a]	$45.8_{(n=131)}$	$70.7_{(n=239)}$
Chance child could be a carrier (verbal)		
Extremely high	$100.0_{(n=4)}$	$77.8_{(n=9)}$
High	$76.5_{(n=17)}$	$88.5_{(n=26)}$
Medium	$52.9_{(n=68)}$	$80.8_{(n=99)}$
Low	$51.8_{(n=54)}$	$73.3_{(n=90)}$
Extremely low	$37.5_{(n=24)}$	$60.9_{(n=46)}$
Chance child could be a carrier (numeric)		
1 in 1 to 1 in 9	$69.0_{(n=29)}$	$75.6_{(n=45)}$
1 in 10 to 1 in 99	$54.0_{(n=50)}$	$79.6_{(n=54)}$
1 in 100 to 1 in 1,000,000[a]	$46.8_{(n=94)}$	$71.2_{(n=184)}$
Chance child could have CF disease (verbal)		
Extremely high/high	$38.5_{(n=13)}$	$70.8_{(n=24)}$
Medium	$53.1_{(n=49)}$	$83.3_{(n=78)}$
Low	$60.6_{(n=66)}$	$69.3_{(n=101)}$
Extremely low	$47.4_{(n=38)}$	$71.6_{(n=67)}$
Chance child could have CF disease (numeric)		
1 in 1 to 1 in 9	$70.0_{(n=20)}$	$83.3_{(n=30)}$
1 in 10 to 1 in 99	$60.0_{(n=35)}$	$72.3_{(n=47)}$
1 in 100 to 1 in 999	$62.9_{(n=35)}$	$81.5_{(n=54)}$
1 in 1,000 to 1 in 1,000,000[a]	$38.6_{(n=83)}$	$69.1_{(n=152)}$

*All analyses were significant for either or both the clinic and home-testing sites.
[a]Subjects who were missing data for this variable were included with this category of respondents.

ject, and use of a saline rinse rather than a blood sample for testing), there is significant, but not universal interest in CF carrier testing among relatives. Home-based education and testing increase acceptance significantly.

A corollary objective of this study was to identify factors related to the acceptance of CF carrier testing for each site. The exploratory regression analyses suggest that, in part, factors commonly associated with general health services utilization were associated with the acceptance of CF carrier education and testing offered in this study [Cockerham, 1978]. More specifically, for both sites, relatives with higher incomes, more education, and those who were female were more likely to accept the offer of education and testing than relatives without these characteristics.

At the same time, the regression analyses suggested that the greater the perceived chance of being a carrier, as well as the greater the perceived chance that a future child could be a carrier, the more likely relatives were to accept education and testing. The questions on perceived chances were asked so relatives could provide both a numerical estimate, i.e., 1 in 10, as well as a verbal assessment of their perceived chance, i.e., high, moderate, low, etc. Perceived numerical chance of personal carrier status and perceived verbal assessment of their child's chance of being a carrier were predictors of acceptance of education and testing for both the home and clinic groups. Perceived chance, or risk, is a common predictor of participation in many medical screening programs and has been found in other studies of genetic testing and counseling to be a predictor of participation as well [Genetic Screening, 1975]. However, it is worth noting that neither perceived burden of having a child with CF nor perceived threat (the combined effect of perceived chance of hav-

TABLE III. Final Clustered Logistic Regression Models for Each Testing Site

	Clinic$_{(N=161)}$		Home$_{(N=266)}$	
	Odds ratio	95% CI	Odds ratio	95% CI
Wanting more children	1.78	(1.19,2.65)	1.67	(1.17,2.40)
Higher income	1.76	(1.26,2.44)	1.86	(1.29,2.68)
Greater education	1.48	(1.01,2.16)	2.04	(1.14,3.65)
Being female	1.71	(0.67,4.37)	2.35	(1.20,4.57)
Higher perceived risk of being a carrier (numeric)	2.15	(1.12,5.18)	1.78	(0.60,5.32)
Higher perceived risk child could be a carrier (verbal)	1.57	(1.07,2.32)	1.30	(0.85,1.98)
CF relative is treated in the pediatric clinic	3.43	(1.44,8.18)	—	—
Less time to drive to UNC Hospitals	1.20	(1.08,1.33)	—	—
Has a spouse or partner	—	—	2.27	(1.13,4)
Goodman-Kruskal gamma	G = 0.593		G = 0.507	

ing a child with CF and perceived burden) was significantly related to accepting education and testing. Finally, in terms of common factors shaping acceptance of education and testing in both sites, relatives who were planning to have a child were more likely to accept education and testing than those who were not. As has been reported in other genetic screening and counseling programs, participation in such programs is partially dependent on whether individuals have completed their families.

The regression analyses also indicate that there were unique factors associated with acceptance of education and testing for each site. For example, for relatives assigned to the clinic site, having the CF patient followed in the pediatric clinic as well as having a shorter drive time to the clinic were both associated with increased participation, whereas neither was significant for relatives assigned to the home site. It is not surprising that the less time they had to spend driving to the clinic the more likely relatives were to accept clinic-based education and testing. Travel time, of course, was not a factor for those whose education and testing took place in the home. The observation that those relatives in the clinic site who had a CF relative being followed in the pediatric as opposed to the adult CF clinic were more likely to participate is not as easy to interpret. It may be that the relatives of pediatric CF patients are especially motivated to participate in all kinds of research, even if it means traveling some distance, hoping their participation may help their young relative in some way.

In the home-based site, in addition to the predictors common to both settings, having a spouse or partner was associated with the acceptance of education and testing. This was not the case for the clinic education and testing site.

There are several limitations that restrict our ability to generalize the results of this study. First, the population in this study were all relatives of a panel of some 120 CF patients who were receiving care at one CF clinic. The patients seen in this clinic may or may not be representative of CF patients nationally. In addition, the population in this study had to live within a 5-state area, be at least 18 years of age, not be pregnant, and able to be interviewed by telephone. These criteria, as well as our inability to contact a substantial number of both CF families as well as relatives, undoubtedly reduce the representativeness of our sample.

We did have requests to test relatives other than those designated in our study protocol, particularly children and some grandparents. Hence, our estimates of the overall level of interest in CF carrier testing among relatives has to be viewed in light of the limitations imposed by study inclusion/exclusion criteria.

Also, it is important to keep in mind that the education and testing offered in this study were free to participants. We adopted this strategy to reduce the effects of economic costs on the acceptance or rejection of CF carrier education and testing. Because of this strategy, our estimates of the level of interest in CF carrier testing among relatives of individuals with CF may in fact be high compared with a situation where relatives have to pay for the services.

It also should be noted that we provided the relatives with limited time in which the study would provide CF carrier education and testing. For some relatives, CF carrier education and testing may have seemed reasonable and useful when we contacted them, while for others it may not have been. For example, relatives who have completed their families, those who are in the process of completing theirs, as well as those who have not really begun to think about having children, may have widely varying interests in CF carrier education and testing, even if they are free of charge. The observation that one factor in our final regression model associated with accepting or rejecting CF carrier education and testing was whether the relative wanted more children adds credence to this consideration.

Finally, the recruitment strategy we employed in this study was an "active" outreach effort where we contacted relatives directly and reduced greatly the need for them to seek information about CF carrier education and testing on their own. It is possible that had a more "passive" approach been employed in contacting relatives, the rate of acceptance would have been less. Nevertheless, the rate of acceptance of CF carrier education and testing in this study is markedly higher than participation rates reported in some population-based pilot testing programs [Tambor et al., 1994], and comparable to that reported in several of the studies of CF carrier testing among relatives cited above. In sum, from this study it appears that the availability of free direct mutation CF carrier education and testing leads to substantial, but not universal acceptance among at-risk relatives.

ACKNOWLEDGMENTS

This work was supported by grant RO1-HG00643 from the National Center for Human Genome Research, National Institutes of Health. The authors acknowledge the contributions of S. Talton, S. Atkins, D. Lewis, A. Bruning, and J. Taylor, as well as the assistance of the UNC-CH Cystic Fibrosis Center.

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